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| Substitute for form 1449A/PTO<br>(Modified)<br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>(use as many sheets as necessary) |   |    |   | <b>Complete if Known</b> |                               |
|  |   |    |   | Application Number       | 10/772,768                    |
|  |   |    |   | Filing Date              | February 4, 2004              |
|  |   |    |   | First Named Inventor     | David A. HORWITZ              |
|  |   |    |   | Art Unit                 | 1644                          |
|  |   |    |   | Examiner Name            | Not Yet Assigned SANJOO JALLA |
| Sheet  | 1 | of | 9 | Attorney Docket Number   | A-68983-2                     |

**U.S. PATENT DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | U.S. Patent Document Number-Kind Code <sup>2</sup> (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|--------------------|-----------------------|---|-----------------------------|---|---|
| ✓                  | A1                    | US 6,228,359 B1   | 05-08-2001                  | Horwitz   |   |
|                    | A2                    | US 6,358,506 B1   | 03-19-2002                  | Horwitz   |   |
|                    | A3                    | US 6,406,696 B1   | 06-18-2002                  | Bluestone                                       |   |
|                    | A4                    | US 6,447,765 B1   | 09-10-2002                  | Horwitz   |   |
|                    | A5 *                  | US 6,797,267 B2   | 09-28-2004                  | Horwitz   |   |
|                    | A6 *                  | US 6,803,036 B1   | 10-12-2004                  | Horwitz   |   |
|                    | A7 *                  | US 6,759,035 B2   | 07-06-2004                  | Horwitz   |   |
|                    | A8 *                  | US 2003/0012791 A1  | 01-16-2003                  | Horwitz   |   |
|                    | A9 *                  | US 2003/0039650 A1  | 02-27-2003                  | Gruenberg                                       |   |
|                    | A10 *                 | US 2003/0157057 A1  | 08-21-2003                  | Horwitz   |   |
| ✓                  | A11 *                 | US 2004/0071667 A1  | 04-15-2004                  | Horwitz   |   |

**FOREIGN PATENT DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Foreign Patent Document Country Code <sup>2</sup> Number <sup>3</sup> Kind Code <sup>5</sup> (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T <sup>4</sup> |
|--------------------|-----------------------|---|-----------------------------|---|---|----------------|
| ✓                  | B1                    | WO 93/17698 A1  | 09-16-1993                  | Schering Corporation                            |   |                |
| ✓                  | B2                    | WO 97/42324 A1  | 11-13-1997                  | Schering Corporation                            |   |                |
| ✓                  | B3                    | WO 99/25366 A1  | 05-27-1999                  | University of Southern California               |   |                |
| ✓                  | B4                    | WO 99/48524 A1  | 09-30-1999                  | University of Southern California               |   |                |
| ✓                  | B5 *                  | WO 00/00587 A1  | 01-06-2000                  | Kaltoft et al.                                  |   |                |
| ✓                  | B6                    | WO 00/66158 A2  | 11-09-2000                  | University of Southern California               |   |                |
| ✓                  | B7                    | WO 01/16296 A2  | 03-08-2001                  | University of Southern California               |   |                |
| ✓                  | B8 *                  | WO 01/77299 A2, A3  | 10-18-2001                  | University of Southern California               |   |                |
| ✓                  | B9 *                  | WO 2003/059264 A3   | 07-24-2003                  | University of Southern California               |   |                |

**NON PATENT LITERATURE DOCUMENTS**

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| ✓                  | C1                    | ANASETTI et al., "Treatment of acute graft-versus-host disease with a nonmitogenic anti-CD3 monoclonal antibody", Transplantation 54:844-851 (1992).  |                |

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| Examiner Signature | <i>Sergiu</i> | Date Considered | 2/9/06 |
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|-------------------------------------|-----------|--|--|--|---------------------------|
| <input checked="" type="checkbox"/> | C2        | ASAI O, et al., "Suppression of graft-versus-host disease and amplification of graft-versus-tumor effects by activated natural killer cells after allogeneic bone marrow transplantation," <i>Journal of Clinical Investigation</i> 101(9):1835-1842 (1998).                   |  |  |                           |
| <input checked="" type="checkbox"/> | C3        | ASANO M, et al., "Autoimmune disease as a consequence of developmental abnormality of a T cell subpopulation." <i>J Exp Med.</i> , 184(2):387-96 (1996 Aug 1).   |  |  |                           |
| <input checked="" type="checkbox"/> | C4        | AUCHINCLOSS, Hugh Jr., et al, in <i>Fundamental Immunology</i> 4th Ed., Paul, W.E. (ed.) Lippincot-Raven: Philadelphia, New York; 1999 pp. 1182-1222.  |  |  |                           |
| <input checked="" type="checkbox"/> | C5        | BARKER et al., "Identification of multiple and distinct CD8+ T cell suppressor activities: dichotomy between infected and uninfected individuals, evolution with progression of disease, and sensitivity to gamma irradiation," <i>J Immunol</i> 156:4476-4483 (1996).         |  |  |                           |
| <input checked="" type="checkbox"/> | C6        | BETZ, M. and FOX, B.S., "Prostaglandin E2 Inhibits production of Th1 lymphokines but not of Th2 lymphokines," <i>J Immunol.</i> , 146(1):108-13 (1991 Jan 1).  |  |  |                           |
| <input checked="" type="checkbox"/> | C7        | BLAZAR et al., "Both CD4+ and CD8+ T Cells Can Cause Accelerated GVHD Lethality in the Presence of High In Vivo Doses of Exogenous IL10: Role of Interferon Gamma (IFN $\gamma$ ) in GVHD Induction," <i>Blood</i> , 88:247 (1996) (abstract)                                  |  |  | Source<br>incorrect       |
| <input checked="" type="checkbox"/> | C8        | BLAZAR et al., "FK506 inhibits graft-versus-host disease and bone marrow graft rejection in murine recipients of MHC disparate donor grafts by interfering with mature peripheral T cell expansion post-transplantation", <i>J. Immunol</i> 153:1836-1846 (1994).              |  |  |                           |
| <input checked="" type="checkbox"/> | C9        | BLAZAR et al., "Murine recipients of fully mismatched donor marrow are protected from lethal graft-versus-host disease by the in vivo administration of rapamycin but develop an autoimmune-like syndrome", <i>J. Immunol</i> 151:5726-5741 (1993).                            |  |  |                           |
| <input checked="" type="checkbox"/> | C10       | BLAZAR et al., "Recent advances in graft-versus-host disease (GVHD)", <i>Immunol Rev</i> 157:79-90 (1997).   |  |  |                           |
| <input checked="" type="checkbox"/> | C11       | BONIG et al., "Transforming Growth Factor- $\beta$ Suppresses Interleukin-15-Mediated Interferon- $\gamma$ Production in Human T Lymphocytes," <i>Scand. J Immunol</i> , 50:612-618 (December 1999).   |  |  |                           |
| <input checked="" type="checkbox"/> | C12       | BONINI et al., "HSV-TK gene transfer into donor lymphocytes for control of allogeneic graft-versus-leukemia, <i>Science</i> 276:1719-1724 (1997).  |  |  |                           |
| <input checked="" type="checkbox"/> | C13       | BORDER et al., "Transforming growth factor-beta in disease: the dark side of tissue repair," <i>J Clin Invest</i> 90:1-7 (1992)  |  |  |                           |
| <input checked="" type="checkbox"/> | C14       | BOUSSIOTIS et al., "B7 but not intercellular adhesion molecule-1 costimulation prevents the induction of human alloantigen-specific tolerance," <i>J Exp Med</i> 178:1753-1763 (1993).   |  |  |                           |
| <input checked="" type="checkbox"/> | C15       | BOUSSIOTIS, "Altered T-cell receptor + CD28-mediated signaling and blocked cell cycle progression in interleukin 10 and transforming growth factor- $\beta$ -treated alloreactive T cells that do not induce graft-versus-host disease," <i>Blood</i> , 97:565-571 (Jan 2001). |  |  |                           |
| <input checked="" type="checkbox"/> | C16       | BUZY, R.P. et al., <i>FASEB J.</i> 1995;9:A497 (Abstract)  |  |  | Source &<br>Title missing |
| <input checked="" type="checkbox"/> | C17       | CHANDRASEKAR, B., et al., "Dietary calorie restriction inhibits transforming growth factor-beta (TGF- beta) expression in murine lupus nephritis", 9th International Congress on Immunology, 848 (1995).   |  |  |                           |
| <input checked="" type="checkbox"/> | C18       | CHAVIN et al., "Anti-CD2 mAbs Suppress Cytotoxic Lymphocyte Activity by the Generation of Th2 Suppressor Cells and Receptor Blockade," <i>J Immunol</i> 152:3729-3739 (1994).  |  |  |                           |

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| Sheet  | 3 | of | 9 | Attorney Docket Number   | A-68983-2                       |

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| ✓                  | C19                   | CHEN et al., "T Cells Specific for a Polymorphic Segment of CD45 Induce Graft-Versus-Host Disease with Predominant Pulmonary Vasculitis," <i>J. Immunology</i> , 161:909-918 (1998).  |                |
| ✓                  | C20                   | CHONG P. et al. "Inhibition of protein-kinase C in peripheral blood mononuclear cells of patients with systemic lupus erythematosus: effect on spontaneous immunoglobulin production," <i>Autoimmunity</i> , 10:227-231 (1991).                                 |                |
| ✓                  | C21                   | COSIMI, A.B., et al., "Treatment of acute renal allograft rejection with OKT3 monoclonal antibody," <i>Transplantation</i> , 32(6):535-9 (1981 Dec).  |                |
| ✓                  | C22                   | DEL ROSARIO et al., "Prevention of Graft-Versus-Host Disease by Induction of Immune Tolerance With Ultraviolet B-irradiated Leukocytes In H-2 Disparate Bone Marrow Donor," <i>Blood</i> , 93(10):3558-3564 (May 1999).   |                |
| ✓                  | C23                   | DELGIUDICE, G., et al., "TGF-beta activity is increased in systemic lupus erythematosus (SLE) and progressive systemic sclerosis (PSS)", <i>Arthritis and Rheumatism</i> Vol. 36 (9 Suppl.) p S196(Sept. 1993).   |                |
| ✓                  | C24                   | DOOMS, H. et al., "IL-2 and IL-4 direct the outcome of inappropriate CD4+ T cell stimulation towards apoptosis and energy respectively," <i>European Cytokine Network</i> , 9(3):169 (1998).  |                |
| ✓                  | C25                   | DUMONT et al., "Distinct Mechanisms of Suppression of Murine T Cell Activation by the Related macrolides FK-506 and Rapamycin", <i>J. Immunol</i> 144:251-258 (1990).   |                |
| ✓                  | C26                   | DUPONT, B., "Immunology of hematopoietic stem cell transplantation: a brief review of its history", <i>Immunol Reviews</i> 157:5-12 (1997).   |                |
| ✓                  | C27                   | EARLY et al., "Rapid conversion of naïve to effector T cell function counteracts diminished primary human newborn T cell responses," <i>Clin Exp Immunol</i> , 1163;L527-533, abstract (June 1999).   |                |
| ✓                  | C28                   | FAST, "Generation and characterization of IL-2-activated veto cells", <i>J Immunol</i> 149:1510-1515 (1992).  |                |
| ✓                  | C29                   | FERNANDES, G., et al., "Calorie restriction delays autoimmune murine lupus by differentially modulating oncogenes and TGF- beta-1 expression", 9th International Congress on Immunology., 848 (1995).   |                |
| ✓                  | C30                   | FOWLER et al., "Donor CD4-enriched cells of Th2 cytokine phenotype regulate graft-versus-host disease without impairing allogeneic engraftment in sublethally irradiated mice", <i>Blood</i> 84:3540-3549 (1994).   |                |
| ✓                  | C31                   | GAO Q, et al., "CD4+CD25+ cells regulate CD8 cell anergy in neonatal tolerant mice." <i>Transplantation</i> , 68(12):1891-7 (1999 Dec 27).  |                |
| ✓                  | C32                   | GARDERET et al., "Effective depletion of alloreactive lymphocytes from peripheral blood mononuclear cell preparations," <i>Transplantation</i> , 67(1):124-130 (January 1999).  |                |
| ✓                  | C33                   | GOLDMAN et al., "Bone marrow transplantation for chronic myelogenous leukemia in chronic phase. Increased risk for relapse associated with T-cell depletion", <i>Ann Intern Med</i> 108:806-814 (1988).   |                |
| ✓                  | C34                   | GRATAMA et al., "Treatment of Acute Graft-Versus-Host Disease With Monoclonal Antibody OKT3. Clinical results and effect on circulating T lymphocytes", <i>Transplantation</i> 38(5):469-474 (1984).  |                |
| ✓                  | C35                   | GRAY et al., "Activated Natural Killer Cells Can Induce Resting B Cells to Produce Immunoglobulin," <i>Arthritis &amp; Rheumatism</i> , 37(2)suppl:S279 (1994).<br><br>Source missing   |                |
| ✓                  | C36                   | GRAY et al., "Generation of an Inhibitory Circuit Involving CD8 <sup>+</sup> T Cells, IL-2 and NK Cell-Derived TGF-β: Contrasting Effects of Anti-CD2 and Anti-CD3", <i>J Immunol</i> , 160:2248-2254 (1998).   |                |
| ✓                  | C37                   | GRAY et al., "The Role of Transforming Growth Factor β in the Generation of Suppression: an Interaction Between CD8 <sup>+</sup> T and NK Cells," <i>J Exp Med</i> 180:1937-1942 (1994).  |                |

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|-------------------------------------|-----------------------|---|--|--|--|
| <input checked="" type="checkbox"/> | C38                   | GRIBBEN et al., "Complete blockade of B7 family-mediated costimulation is necessary to induce human alloantigen-specific anergy: a method to ameliorate graft-versus-host disease and extend the donor pool", <i>Blood</i> 97:4887-4893 (1996).                     |  |  |  |
| <input checked="" type="checkbox"/> | C39                   | GROUX, H., et al., "A CD4+ T-cell subset inhibits antigen-specific T-cell responses and prevents colitis," <i>Nature</i> , 389(6652):737-42 (1997 Oct 16).  |  |  |  |
| <input checked="" type="checkbox"/> | C40                   | HAHN, B.H., Dubois' Lupus Erythematosus, 5th Ed. (1997), pp. 69-76 (D.J. Wallace et al. eds., Williams and Wilkins, Baltimore).   |  |  |  |
| <input checked="" type="checkbox"/> | C41                   | HALVERSON et al., "In Vitro Generation of Allospecific Human CD8 <sup>+</sup> T Cells of Tc1 and Tc2 Phenotype," <i>Blood</i> , 90(5):2089-2096 (September 1997).   |  |  |  |
| <input checked="" type="checkbox"/> | C42                   | HAN, et al., "A New Type of CD4+ Suppressor T cell Completely Prevents Spontaneous Autoimmune Diabetes and Recurrent Diabetes in Syngeneic Islet-Transplanted NOD Mice," <i>Journal of Autoimmunity</i> , 9:331-339 (1996).   |  |  |  |
| <input checked="" type="checkbox"/> | C43                   | HEITGER et al., "Essential Role of the Thymus to Reconstitute Naïve (CD45RA <sup>+</sup> ) T-Helper Cells After Human Allogeneic Bone Marrow Transplantation", <i>Blood</i> , 90(2):850-857 (July 1997).  |  |  |  |
| <input checked="" type="checkbox"/> | C44                   | HERVE et al., "Treatment of Corticosteroid-Resistant Acute Graft-Versus-Host Disease by In Vivo Administration of Anti-Interleukin-2 Receptor Monoclonal Antibody (B-B10)", <i>Blood</i> 75(4):1017-1023 (1990). <i>Autko's mis identified</i>                      |  |  |  |
| <input checked="" type="checkbox"/> | C45                   | HIROHATA et al., "Role of IL-2 in the generation of CD4+ suppressors of human B cell responsiveness", <i>J Immunol.</i> , 142:3104-3112 (1989)  |  |  |  |
| <input checked="" type="checkbox"/> | C46                   | HIROKAWA et al., "Human resting B lymphocytes can serve as accessory cells for anti-CD2-induced T cell activation", <i>J. Immunol.</i> , 149:1859-1866, (1992).   |  |  |  |
| <input checked="" type="checkbox"/> | C47                   | HIRUMA et al., "Effects of anti-CD3 monoclonal antibody on engraftment of T-cell-depleted bone marrow allografts in mice: host T-cell suppression, growth factors, and space", <i>Blood</i> 79:3050-3058 (1992)   |  |  |  |
| <input checked="" type="checkbox"/> | C48                   | HORWITZ DA, et al., "Decreased production of interleukin-12 and other Th1-type cytokines in patients with recent-onset systemic lupus erythematosus." <i>Arthritis Rheum.</i> , 41(5):838-44 (1998 May).  |  |  |  |
| <input checked="" type="checkbox"/> | C49                   | HORWITZ, D. A., et al., "The immunoregulatory effects of NK cells: the role of TGF- $\beta$ and implications for autoimmunity", <i>Immunology Today</i> , Vol. 18(11):538-542 (Nov. 1997).  |  |  |  |
| <input checked="" type="checkbox"/> | C50                   | HORWITZ, D.A., Dubois' Lupus Erythematosus, 5th Ed. (1997), pp. 155-194 (D.J. Wallace et al. eds., Williams and Wilkins, Baltimore).  |  |  |  |
| <input checked="" type="checkbox"/> | C51                   | HUGGINS, M. L., et al., "Modulation of the Autoimmune Response in Lupus Mice by Oral Administration of Attenuated <i>Salmonella typhimurium</i> Expressing the IL-2 and TGF- $\beta$ Genes", <i>Annals of New York Acad. of Sciences</i> , Vol. 815:499-502 (1997). |  |  |  |
| <input checked="" type="checkbox"/> | C52                   | JACKSON AL, et al., "Restricted expression of p55 interleukin 2 receptor (CD25) on normal T cells." <i>Clin Immunol Immunopathol.</i> , 54(1):126-33 (1990 Jan).  |  |  |  |
| <input checked="" type="checkbox"/> | C53                   | JONULEIT, H., et al., "Induction of interleukin 10-producing, nonproliferating CD4(+) T cells with regulatory properties by repetitive stimulation with allogeneic immature human dendritic cells," <i>J Exp Med.</i> , 192(9):1213-22 (2000 Nov 6).                |  |  |  |
| <input checked="" type="checkbox"/> | C54                   | KANEYANE H, et al., "A novel subpopulation of CD45RA <sup>+</sup> CD4+ T cells expressing IL-2 receptor alpha-chain (CD25) and having a functionally transitional nature into memory cells." <i>Int Immunol.</i> , 3(12):1349-56 (1991 Dec).                        |  |  |  |

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| Examiner Signature | <i>Jayn</i> | Date Considered | 2/9/06 |
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|   |   |    |   | Filing Date              | February 4, 2004                |
|   |   |    |   | First Named Inventor     | David A. HORWITZ                |
|   |   |    |   | Art Unit                 | 1644                            |
|   |   |    |   | Examiner Name            | Not Yet Assigned - SANTOO TALLA |
| Sheet                                       | 5 | of | 9 | Attorney Docket Number   | A-68983-2                       |

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| ✓                  | C55                   | KINTER et al., "Interleukin 2 induces CD8+ T cell-mediated suppression of human immunodeficiency virus replication in CD4+ T cells and this effect overrides its ability to simulate virus expression", <i>Proc. Natl. Acad. Sci. USA</i> 92:10985-10989 (1995).                       |                |
|                    | C56                   | KIRK, A.D., et al., "CTLA4-Ig and anti-CD40 ligand prevent renal allograft rejection in primates," <i>Proc Natl Acad Sci U S A</i> , 94(16):8789-94 (1997 Aug 5).  |                |
|                    | C57                   | KLINMAN DM, et al., "Quantitation of IgM- and IgG-secreting B cells in the peripheral blood of patients with systemic lupus erythematosus." <i>Arthritis Rheum.</i> , 34(11):1404-10 (1991 Nov).   |                |
|                    | C58                   | KOH et al., "Adoptive cellular immunotherapy: NK cells and bone marrow transplantation," <i>Histol Histopathol.</i> , 15:1201-1210 (2000).   |                |
|                    | C59                   | KOIDE, J. and ENGLEMAN, E.G., "Differences in surface phenotype and mechanism of action between alloantigen-specific CD8+ cytotoxic and suppressor T cell clones," <i>J Immunol.</i> , 144(1):32-40 (1990 Jan 1).  |                |
|                    | C60                   | KRENGER et al., "Effects of exogenous interleukin-10 in a murine model of graft-versus-host disease to minor histocompatibility antigens", <i>Transplantation</i> 58:1251-1257 (1994).   |                |
|                    | C61                   | KRENGER et al., "Polarized type 2 alloreactive CD4+ and CD8+ donor T cells fail to induce experimental acute graft-versus-host disease", <i>J Immunol</i> 153:585-593 (1995).  |                |
|                    | C62                   | LANCASTER, F., et al., "Anti-idiotypic T cells suppress rejection of renal allografts in rats," <i>Nature</i> ., 1985 May 23-29;315(6017):336-7.   |                |
|                    | C63                   | LANGREHR, J.M., et al., "Evidence that nitric oxide production by in vivo allosensitized cells inhibits the development of allospecific CTL," <i>Transplantation</i> , 53(3):632-40 (1992 Mar).  |                |
|                    | C64                   | LARSEN, C.P., et al., "Long-term acceptance of skin and cardiac allografts after blocking CD40 and CD28 pathways," <i>Nature</i> , 381(6581):434-8 (1996 May 30).  |                |
|                    | C65                   | LINKER-ISRAELI M, et al., "CD8+ lymphocytes from patients with systemic lupus erythematosus sustain, rather than suppress, spontaneous polyclonal IgG production and synergize with CD4+ cells to support autoantibody synthesis." <i>Arthritis Rheum.</i> , 33(8):1216-25 (1990 Aug). |                |
|                    | C66                   | LUCAS et al., "The development of cellular immunity to Epstein-Barr virus after allogeneic bone marrow transplantation", <i>Blood</i> 87:2594-2603 (1996).   |                |
|                    | C67                   | MARTIN et al., "Effects of in vitro depletion of T cells in HLA-identical allogeneic marrow grafts", <i>Blood</i> 66:664-672 (1985).   |                |
|                    | C68                   | MARTIN et al., "Effects of treating marrow with a CD3-specific immunotoxin for prevention of acute graft-versus-host disease", <i>Bone Marrow Transplant</i> 3:437-444 (1989).   |                |
|                    | C69                   | MARTIN, "Overview of Marrow Transplantation Immunology", in <i>Bone Marrow Transplantation</i> (eds. Forman et al.) pp. 16-21, Boston, Blackwell Scientific Publications (1994).   |                |
|                    | C70                   | MARTIN, P.J. et al., "Treatment of Acute Graft-Versus-Host Disease with Anti-CD3 Monoclonal Antibodies," <i>Am Jour Kidney Disease</i> 11(2):149-152 (1988).   |                |
| ✓                  | C71                   | MASSAGUE J., "The transforming growth factor-beta family." <i>Annu Rev Cell Biol.</i> , 6:597-641 (1990).  |                |
| ✓                  | C72                   | MASSAGUE, "Receptors for the TGF-beta family", <i>Cell</i> 69:1067-1070 (1992).  |                |

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| Examiner Signature | <i>Santoo</i> | Date Considered | 2/9/06 |
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| Sheet   | 6 | of | 9 | Application Number       | 10/772,768                    |
|   |   |    |   | Filing Date              | February 4, 2004              |
|   |   |    |   | First Named Inventor     | David A. HORWITZ              |
|   |   |    |   | Art Unit                 | 1644                          |
|   |   |    |   | Examiner Name            | Not Yet Assigned SANJOO JALLA |
|   |   |    |   | Attorney Docket Number   | A-68983-2                     |

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| <input checked="" type="checkbox"/> | C73                   | MIZUOCHI, T., et al., "Both L3T4+ and Lyt-2+ helper T cells initiate cytotoxic T lymphocyte responses against allogenic major histocompatibility antigens but not against trinitrophenyl-modified self," <i>J Exp Med.</i> , 62(2):427-43 (1985 Aug 1).   |  |  |                                 |
| <input checked="" type="checkbox"/> | C74                   | MORRIS, "Prevention and treatment of allograft rejection in vivo by rapamycin: molecular and cellular mechanisms of action", <i>Ann NY Acad Sci</i> 685:68-72 (1993).   |  |  |                                 |
| <input checked="" type="checkbox"/> | C75                   | MURPHY et al, "The potential role of NK cells in the separation of graft-versus-tumor effects from graft-versus-host disease after allogeneic bone marrow transplantation," <i>Immunol Rev</i> 157:167-176 (1997).  |  |  |                                 |
| <input checked="" type="checkbox"/> | C76                   | MYSLIWETZ et al., "Antilymphocytic antibodies and marrow transplantation. XII. Suppression of graft-versus-host disease by T cell-modulating-and-depleting-antimouse-CD3 antibody is most effective when preinjected in the marrow-recipient," <i>Blood</i> , 88(10):2661-2667, abstract (November 1992). |  |  | Ref.<br>could not<br>be located |
| <input checked="" type="checkbox"/> | C77                   | OHTSUKA, K., et al., "Decreased Production of TGF- $\beta$ by Lymphocytes from Patients with Systemic Lupus Erythematosus", <i>J. Immunol.</i> , 160:2539-2545 (1998).  |  |  |                                 |
| <input checked="" type="checkbox"/> | C78                   | OSWALD, et al., "IL-10 Synergizes with IL-4 and Transforming Growth Factor-Beta to Inhibit macrophage Cytotoxic Activity," <i>J Immunology</i> 148(11):3578-3582 (1992).  |  |  | Ref. Could<br>not be located    |
| <input checked="" type="checkbox"/> | C79                   | PAPIERNIK M, et al., "T cell deletion induced by chronic infection with mouse mammary tumor virus spares a CD25-positive, IL-10-producing T cell population with infectious capacity." <i>J Immunol.</i> , 158(10):4642-53 (1997 May 15).   |  |  |                                 |
| <input checked="" type="checkbox"/> | C80                   | PATTERSON et al., "Graft rejection following HLA matched T-lymphocyte depleted bone marrow transplantation", <i>Br J Haematol</i> 63:221-230 (1986).  |  |  |                                 |
| <input checked="" type="checkbox"/> | C81                   | PAWELEC, et al., "Cytokine Modulation of TH1/TH2 Phenotype Differentiation in Directly Alloresponsive CD4+ Human T Cells," <i>Transplantation</i> , 62(8):1095-1101 (October 1996).   |  |  |                                 |
| <input checked="" type="checkbox"/> | C82                   | PEARCE, N.W., et al., "Specific unresponsiveness in rats with prolonged cardiac allograft survival after treatment with cyclosporine. V. Dependence of CD4+ suppressor cells on the presence of alloantigen and cytokines, including interleukin 2," <i>Transplantation</i> , 55(2):374-80 (1993 Feb).    |  |  |                                 |
| <input checked="" type="checkbox"/> | C83                   | PESCOVITZ, M.D., et al., "Effect of class II antigen matching on renal allograft survival in miniature swine," <i>J Exp Med.</i> , 160(5):1495-508 (1984 Nov 1).  |  |  |                                 |
| <input checked="" type="checkbox"/> | C84                   | POWRIE F, et al., "A critical role for transforming growth factor-beta but not interleukin 4 in the suppression of T helper type 1-mediated colitis by CD45RB(low) CD4+ T cells." <i>J Exp Med.</i> , 183(6):2669-74 (1996 Jun 1).  |  |  |                                 |
| <input checked="" type="checkbox"/> | C85                   | QIN, L., et al., "Gene transfer for transplantation. Prolongation of allograft survival with transforming growth factor-beta 1," <i>Ann Surg.</i> , 220(4):508-18; discussion 518-9 (1994 Oct).   |  |  |                                 |
| <input checked="" type="checkbox"/> | C86                   | QIN, L., et al., "Retrovirus-mediated transfer of viral IL-10 gene prolongs murine cardiac allograft survival," <i>J Immunol.</i> , 156(6):2316-23 (1996 Mar 15).   |  |  |                                 |
| <input checked="" type="checkbox"/> | C87                   | RAJU, G.P., et al., "Prolongation of cardiac allograft survival with transforming growth factor-beta 1 in rats," <i>Transplantation</i> , 58(3):392-6 (1994 Aug 15).  |  |  |                                 |
| <input checked="" type="checkbox"/> | C88                   | RAMSDELL, F. and FOWLKES, B.J., "Maintenance of in vivo tolerance by persistence of antigen," <i>Science</i> , 257(5073):1130-4 (1992 Aug 21).  |  |  |                                 |
| <input checked="" type="checkbox"/> | C89                   | READ S, et al., "Cytotoxic T lymphocyte-associated antigen 4 plays an essential role in the function of CD25(+)/CD4(+) regulatory cells that control intestinal inflammation." <i>J Exp Med.</i> , 192(2):295-302 (2000 Jul 17).  |  |  |                                 |

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|  |   |    |   | Filing Date              | February 4, 2004              |
|  |   |    |   | First Named Inventor     | David A. HORWITZ              |
|  |   |    |   | Art Unit                 | 1644                          |
|  |   |    |   | Examiner Name            | Not Yet Assigned SANJOO TALLA |
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| <input checked="" type="checkbox"/> | C90                   | ROCHA, B., et al., "Clonal anergy blocks in vivo growth of mature T cells and can be reversed in the absence of antigen," <i>J Exp Med.</i> , 177(5):1517-21 (1993 May 1).   |  |  |  |
| <input type="checkbox"/>            | C91                   | RODT, H., "Anti-lymphocytic antibodies and marrow transplantation. 3. Effect of heterologous anti-brain antibodies on acute secondary disease in mice", <i>Eur. J. Immunol.</i> , 4:25-29 (1974).  |  |  |  |
| <input type="checkbox"/>            | C92                   | ROOK et al., "Effects of Transforming Growth Factor $\beta$ on the Functions of Natural Killer Cells: Depressed Cytolytic Activity and Blunting of Interferon Responsiveness," <i>J Immunology</i> 136(10):3916-3920 (1986).   |  |  |  |
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| <input type="checkbox"/>            | C94                   | SAKAGUCHI S, et al., "Organ-specific autoimmune diseases induced in mice by elimination of T cell subset. I. Evidence for the active participation of T cells in natural self-tolerance; deficit of a T cell subset as a possible cause of autoimmune disease." <i>J Exp Med.</i> , 161(1):72-87 (1985 Jan 1). |  |  |  |
| <input type="checkbox"/>            | C95                   | SAKAGUCHI, S., et al., "Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases," <i>J Immunol.</i> , 155(3):1151-64 (1995 Aug 1).                                       |  |  |  |
| <input type="checkbox"/>            | C96                   | SEDDON, B. and MASON, D., "The third function of the thymus," <i>Immunol Today</i> , 21(2):95-9 (2000 Feb).  |  |  |  |
| <input type="checkbox"/>            | C97                   | SHEVACH, E.M., "Regulatory T cells in autoimmunity," <i>Annu Rev Immunol.</i> , 18:423-49 (2000).  |  |  |  |
| <input type="checkbox"/>            | C98                   | SHIVAKUMAR S, et al., "T cell receptor alpha/beta expressing double-negative (CD4-/CD8-) and CD4+ T helper cells in humans augment the production of pathogenic anti-DNA autoantibodies associated with lupus nephritis." <i>J Immunol.</i> , 143(1):103-12 (1989 Jul 1).                                      |  |  |  |
| <input type="checkbox"/>            | C99                   | SINGER, A., et al., "Self recognition in allogeneic radiation bone marrow chimeras. A radiation-resistant host element dictates the self specificity and immune response gene phenotype of T-helper cells," <i>J Exp Med.</i> , 153(5):1286-301 (1981 May 1).  |  |  |  |
| <input type="checkbox"/>            | C100                  | SNIJDEWINT, F.G., et al., "Prostaglandin E2 differentially modulates cytokine secretion profiles of human T helper lymphocytes," <i>J Immunol.</i> , 150(12):5321-9 (1993 Jun 15).   |  |  |  |
| <input type="checkbox"/>            | C101                  | SPORN et al., "Some recent advances in the chemistry and biology of transforming growth factor-beta," <i>J Cell Biol</i> 105:1039-1045 (1987).   |  |  |  |
| <input type="checkbox"/>            | C102                  | STARZL, T.E., et al., "Chimerism and donor-specific nonreactivity 27 to 29 years after kidney allotransplantation," <i>Transplantation</i> , 55(6):1272-7 (1993 Jun).  |  |  |  |
| <input type="checkbox"/>            | C103                  | STORB et al., "Long-term follow-up of a controlled trial comparing a combination of methotrexate plus cyclosporine with cyclosporine alone for prophylaxis of graft-versus-host disease in patients administered HLA-identical marrow grafts for leukemia", <i>Blood</i> 80:560-561 (1992)                     |  |  |  |
| <input type="checkbox"/>            | C104                  | STRAND, V., "Approaches to the management of systemic lupus erythematosus," <i>Current Opinion in Rheumatology</i> , 9:410-420 (1997).   |  |  |  |
| <input checked="" type="checkbox"/> | C105                  | SULLIVAN et al., "Chronic Graft-Versus-Host Disease and Other Late Complications of Bone Marrow Transplantation", <i>Semin Hematol</i> 28:250-259 (1992).  |  |  |  |

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|  |   |    |   | First Named Inventor     | David A. HORWITZ                |
|  |   |    |   | Art Unit                 | 1644                            |
|  |   |    |   | Examiner Name            | Not Yet Assigned - SANTOO JALIA |
| Sheet  | 8 | of | 9 | Attorney Docket Number   | A-68983-2                       |

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| ✓                  | C106                  | SURI-PAYER E, et al., "CD4+CD25+ T cells inhibit both the induction and effector function of autoreactive T cells and represent a unique lineage of immunoregulatory cells." <i>J Immunol.</i> , 160(3):1212-8 (1998 Feb 1).   |
| ✓                  | C107                  | SURI-PAYER E, et al., "Post-thymectomy autoimmune gastritis: fine specificity and pathogenicity of anti-H/K ATPase-reactive T cells." <i>Eur J Immunol.</i> , 29(2):669-77 (1999 Feb).   |
| ✓                  | C108                  | SYKES, M. et al., "In Vitro and In Vivo Analysis of Bone Marrow-Derived CD3+, CD4-, CD8-, NK1.1+ Cell Lines." <i>Cell Immunol.</i> , 129(2):478-493 (1990).  |
| ✓                  | C109                  | TAAMS, L.S., et al., "Anergic T cells actively suppress T cell responses via the antigen-presenting cell," <i>Eur J Immunol.</i> , 28(9):2902-12 (1998 Sep).   |
|                    | C110                  | TAKAHASHI T, et al., "Human CD8+ lymphocytes stimulated in the absence of CD4+ cells enhance IgG production by antibody-secreting B cells," <i>Clin Immunol Immunopathol.</i> , 58(3):352-65 (1991 Mar).   |
|                    | C111                  | TAKAHASHI T, et al., "Immunologic self-tolerance maintained by CD25+CD4+ naturally anergic and suppressive T cells: induction of autoimmune disease by breaking their anergic/suppressive state." <i>Int Immunol.</i> , 10(12):1969-80 (1998 Dec).                   |
|                    | C112                  | TAYLOR, "Antigen specific suppressor T cells respond to cytokines released by T cells", <i>Advances Exp Med Biol</i> 319:125-135 (1992).   |
|                    | C113                  | THORNTON AM and Shevach EM. "CD4+CD25+ immunoregulatory T cells suppress polyclonal T cell activation in vitro by inhibiting interleukin 2 production." <i>J Exp Med.</i> , 188(2):287-96 (1998 Jul 20).   |
|                    | C114                  | THORNTON AM and Shevach EM. "Suppressor effector function of CD4+CD25+ immunoregulatory T cells is antigen nonspecific." <i>J Immunol.</i> , 164(1):183-90 (2000 Jan 1).   |
|                    | C115                  | TOMITA, Y., et al., "Importance of suppressor T cells in cyclophosphamide-induced tolerance to the non-H-2-encoded alloantigens. Is mixed chimerism really required in maintaining a skin allograft tolerance?" <i>J Immunol.</i> , 144(2):463-73 (1990 Jan 15).     |
|                    | C116                  | VALLERA et al., "Bone marrow transplantation across major histocompatibility barriers in mice. Effect of elimination of T cells from donor grafts by treatment with monoclonal Thy-1.2 plus complement or antibody alone", <i>Transplantation</i> 31:218-222 (1981). |
|                    | C117                  | VENDETTI, S., et al., "Anergic T cells inhibit the antigen-presenting function of dendritic cells," <i>J Immunol.</i> , 165(3):1175-81(2000 Aug 1).  |
|                    | C118                  | VERBANAC, K.M., et al., "A role for transforming growth factor-beta in the veto mechanism in transplant tolerance," <i>Transplantation</i> , 57(6):893-900 (1994 Mar 27).  |
|                    | C119                  | VIA et al., "Critical Role of interleukin-2 in the development of acute graft-versus-host disease", <i>International Immunol</i> 5:565-572 (1993).   |
|                    | C120                  | WAHL SM. "Transforming growth factor beta: the good, the bad, and the ugly." <i>J Exp Med.</i> , 180(5):1587-90 (1994 Nov 1).  |
|                    | C121                  | WEINER HL, et al., "Oral tolerance: immunologic mechanisms and treatment of animal and human organ-specific autoimmune diseases by oral administration of autoantigens." <i>Annu Rev Immunol.</i> , 12:809-37 (1994).  |
| ✓                  | C122                  | WEKERLE, T., et al., "Anti-CD154 or CTLA4Ig obviates the need for thymic irradiation in a non-myeloablative conditioning regimen for the induction of mixed hematopoietic chimerism and tolerance." <i>Transplantation</i> , 68(9):1348-55 (1999 Nov 15).            |

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|   |   |    |   | Application Number       | 10/772,768                   |
|   |   |    |   | Filing Date              | February 4, 2004             |
|   |   |    |   | First Named Inventor     | David A. HORWITZ             |
|   |   |    |   | Art Unit                 | 1644                         |
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| <i>S</i>           | C123                  | WILSON, D.B., "Idiotypic regulation of T cells in graft-versus-host disease and autoimmunity," <i>Immunol Rev.</i> , 107:159-77 (1989 Feb).   |                |
| <i>S</i>           | C124                  | ZEHAVI-WILLNER et al., "The Mitogenic Activity of Staphylococcal Enterotoxin B (SEB): A Monovalent T Cell Mitogen That Stimulates Cytolytic T Lymphocytes but Cannot Mediate Their Lytic Interaction," <i>Journal of Immunology</i> 127(8):2682-2687 (1986).  |                |
| <i>S</i>           | C125                  | ZELLER et al., "Induction of CD4+ T Cell Alloantigen-Specific Hyporesponsiveness by IL-10 and TGF- $\beta$ ", <i>Journal of Immunology</i> 163:3684-3691 (1999).  |                |
|                    | C126                  | ZELLER, et al., "Ex vivo IL-10 and TGF-Beta Act Synergistically to Induce CD4+ Alloantigen-Specific Tolerance Resulting in Diminished Graft-Versus-Host Disease In Vivo," <i>FASEB Journal</i> (March 12, 1999) 12(4)part 1, A814. Meeting Info: Annual Meeting of the Professional Research Scientists for Experimental Biology, April 17-21 1999. | Source missing |
| <i>S</i>           | C127                  | ZHENG, X.X., et al., "Administration of noncytolytic IL-10/Fc in murine models of lipopolysaccharide-induced septic shock and allogeneic islet transplantation," <i>J Immunol</i> , 154(10):5590-600 (1995 May 15).   |                |

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